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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Tsutomu SUZUKI

Group Art Unit : Not Yet Assigned

Appl. No. : 10/541,588
(U.S. National Stage of PCT/JP04/000046)

I.A. Filed : January 7, 2004

Confirmation No. : 1998

For : METHOD FOR PRODUCING siRNA

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop AMENDMENT
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir :

In accordance with the duty of disclosure under 37 C.F.R. §1.56 and §§1.97-1.98, Applicants hereby bring the following information to the attention of the Examiner in charge of the above-identified application, which includes information cited and discussed in the specification and the International Search Report issued in connection with International Patent Application No. PCT/JP04/000046, of which the present application is the U.S. National Stage Application. A copy of the International Search Report was enclosed with the papers when entering the U.S. National Stage on January 7, 2004. The Examiner is invited to review these materials to inspect the relevance indicated during international examination with respect to the documents cited therein.

The following is a list of the documents cited in the above-noted documents:

FIRE, A., et al., Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. *Nature*, 391, 806-1 (1998), that is cited on page 2 of the specification.

FRASER, A.G., et al., Functional genomic analysis of C. elegans chromosome I by systematic RNA interference. *Nature*, 408, 325-30 (2000), that is cited on page 3 of the specification.

GONCZY, P., et al., Functional genomic analysis of cell division in C. elegans using RNAi of genes on chromosome III. *Nature*, 408, 331-6 (2000), that is cited on page 3 of the specification.

MANCHE, L., et al., Interactions between double-stranded RNA regulators and the protein kinase DAI. *Mol Cell Biol*, 12, 5238-48 (1992), that is cited on page 4 of the specification.

MINKS, M. A., et al., Structural requirements of double-stranded RNA for the activation of 2',5'-oligo(A) polymerase and protein kinase of interferon-treated HeLa cells. *J Biol Chem*, 254, 10180-3 (1979), that is cited on page 4 of the specification.

BERNSTEIN, E., et al., Role for a bidentate ribonuclease in the initiation step of RNA interference. *Nature*, 409, 363-6 (2001), that is cited on page 4 of the specification.

ZAMORE, P. D., et al., RNAi: double-stranded RNA directs the ATP-dependent cleavage of mRNA at 21 to 23 nucleotide intervals. *Cell*, 101, 25-33 (2000), that is cited on page 4 of the specification.

HAMMOND, S. M., et al., An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells. *Nature*, 404, 293-6 (2000), that is cited on page 4 of the specification.

LIPARDI, C., et al., RNAi as random degradative PCR: siRNA primers convert mRNA into dsRNAs that are degraded to generate new siRNAs. *Cell*, 107, 297-307 (2001), that is cited on page 4 of the specification.

ELBASHIR, S. M., et al., Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. *Nature*, 411, 494-498 (2001a), that is cited on page x of the specification.

ELBASHIR, S. M., et al., RNA interference is mediated by 21- and 22-nucleotide RNAs. *Genes Dev*, 15, 188-200 (2001b), that is cited on page 5 of the specification.

DONZE, O., et al., RNA interference in mammalian cells using siRNAs synthesized with T7 RNA polymerase. *Nucleic Acids Res*, 30, e46 (2002), that is cited on page 5 of the specification.

YOSHIZAWA S et al., GNA trinucleotide loop sequences producing extraordinarily stable DNA minihairpins. *Biochemistry,* 36(16): 4761-7 (1997), that is cited on page 12 of the specification.

MILLIGAN, J. F., et al., Synthesis of small RNAs using T7 RNA polymerase. *Methods Enzymol*, 180, 51-62 (1989), that is cited on page 14 of the specification.

HIRAO, I., et al., Most compact hairpin-turn structure exerted by a short DNA fragment, d(GCGAAGC) in solution: an extraordinarily stable structure resistant to nucleases and heat. *Nucleic Acids Res*, 22, 576-82 (1994), that is cited on page 14 of the specification.

KATOH, T. et al., Simple and rapid synthesis of siRNA derived from *in vitro* transcribed shRNA, *Nucleic Acids Research Supplemen*t No. 3, pages 249-250 (September 2003).

PADDISON, P.J. et al., Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells, *Genes & Dev.*, Vol. 16, pages 948-958 (2002).

YU, J.Y. et al., RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells, *Proc. Natl. Acad. Sci. USA*, Vol. 99(9), pages 6047-6052 (2002).

MORITA, T. et al., RNAi provides a new tool for functional analyses of the mammalian genes, *Protein, Nucleic Acid, and Enzyme*, Vol. 47(14), pages 1939-1945 (2002).

PAUL, C.P. et al., Effective expression of small interfering RNA in human cells, *Nat. Biotechnol.*, Vol. 20(5), pages 505-508 (2002).

Copies of the above-noted documents are enclosed together with a duly completed Form PTO-1449. The Examiner is accordingly requested to consider

each of these documents, and to make them of record in this application by initialing in the appropriate spaces on the Form PTO-1449. Applicants respectfully request that the Examiner include a copy of the initialed Form PTO-1449 with the next communication from the U.S. Patent and Trademark Office.

Applicants note that an Office Action on the merits has not issued in the present application, and thus no fee is believed necessary to ensure consideration of the submitted material. However, if an Office Action on the merits has issued and is crossing this statement in the mail, the undersigned hereby authorizes the Commissioner to charge any fee necessary for the consideration of this statement, including any payment under 37 C.F.R. §1.17 (p) to Deposit Account No. 19-0089.

Should there be any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,
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FORM PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. P28165	Application No. 10/541,588
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		Applicant Tsutomu SUZUKI	
		I.A. Filing Date January 7, 2004	Group Not Yet Assigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	1	FIRE, A., et al., Potent and specific genetic interference by double- stranded RNA in
		Caenorhabditis elegans. *Nature*, 391, 806-1 (1998).
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		Chem, 254, 10180-3 (1979).
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		mammalian cells. *Nature*, 411, 494-498 (2001a).
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		Genes Dev, 15, 188-200 (2001b).

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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